Journal of Investigative and Clinical Dentistry (2011), **2**, 1–9

ORIGINAL ARTICLE

Oral Biosciences

Craniofacial parameters of Syrian children with β-thalassemia major

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Keywords
cephalometric, craniofacial parameters, malocclusion, Syrian children, β-thalassemia major.

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Received 26 June 2010; accepted 24 October 2010.

doi: 10.1111/j.2041-1626.2010.00042.x

Abstract

Aim: To investigate cephalometric craniofacial parameters (skeletal and dental) of β-thalassemic-major patients and to compare findings with a group of healthy patients in the same age group.

Methods: Fifty-one Syrian thalassemic-major patients aged 8–12 years were recruited. Lateral cephalometric radiographs were taken. Linear and angular cephalometric measurements were recorded and compared with Syrian controls ($n = 50$) in the same age group.

Results: Thalassemic patients, when compared with controls, showed significant retrognathia in the mandible (reduced sella [mid-point of sella turcica]–nasion [most anterior point on the frontonasal suture] B-point [deepest point on the concavity of the mandibular profile between the alveolar crest and the point of the chin] angle, and decreased sella–nasion–pogonion [most anterior point on the bony chin] angle, $P < 0.0001$), a significant decrease in ramus height (articulare–gonian = 36.51 ± 3.87 mm, $P < 0.0001$). They also exhibited a significant class II skeletal pattern ($P < 0.0001$) and a convex facial profile as the nasion A-point (deepest point on maxillary profile between the anterior nasal spine and the alveolar crest) pogonion angle and maxillomandibular A-point–nasion P-point angle increased. They also showed a highly-significant decrease in the total posterior facial height (sella gonion [most posterior, inferior point on the angle of the mandible] = 64.24 ± 5.73 mm, $P < 0.0001$) and significant increase in the total anterior facial height (N–Me = 110.78 ± 6.66 mm, $P = 0.009$) when compared to controls.

Conclusion: Thalassemic patients exhibited a skeletal class II malocclusion, retrognathia of the mandible, a short height of the ramus, an increase in anterior facial height, and a decrease in posterior facial height.

Introduction

There is a diverse group of genetic blood diseases characterized by the absent or decreased production of either α- or β-globulin protein chains, resulting in microcytic anemia of varying degrees, and referred to as α- or β-thalassemia.[1]

The intensity of the clinical manifestations is correlated to the severity of thalassemia.[2] Patients with the most severe form of the disease rarely survive into adulthood because of cardiac failure, chronic anemia, and hypoxia.[1] Liver impairment is mild. Fibrosis is usually present, with infrequent progression towards cirrhosis.[2] Endocrine gland involvement leads to growth retardation and developmental alterations. The skeletal retardation increases with age due to hypoxia from severe anemia, endocrine hypofunction secondary to iron deposition, or the toxic action of iron enzyme systems leading to tissue injury. The appearance of diabetes mellitus with hypothyroidism at older ages is a common finding.[2]

The orofacial manifestations of thalassemia are the result of bony changes occurring due to ineffective erythropoiesis.[3]

It has been reported in the literature that the major oral change in thalassemic patients is the enlargement of the maxilla caused by bone marrow expansion. Overgrowth causes a characteristic appearance known as ''chipmunk fancies''.[4] Caffey described the appearance of these thalassemic patients as resembling a ''rodent face''.[5] Dentofacial manifestations reported in the literature are a protrusive premaxilla associated with alveolar enlargement,[6] flaring and spacing of the upper anterior teeth, increased overjet, and reduced overbite.[7] Indeed, those patients exhibit a prominent malar bone, depression of the bridge of the nose, and a partially obliterated maxillary sinus.[6] In addition, the pneumatization of the maxillary sinuses is delayed and the upper lip is retracted.[3,7] Anemia has been implicated in the retardation of the condylar and ramal growth of the mandible. Class II skeletal pattern with bimaxillary protrusion and a pronounced vertical growth direction of the mandible have been observed. The mandible is smaller in size and more retruded in the face among thalassemic patients.[8]

This disease is broadly distributed throughout parts of Africa, the Mediterranean region, the Middle East, the Indian subcontinent, South-East Asia, and islands of the Pacific, and it occurs sporadically in all racial groups.[9] In Saudi Arabia, more than 50% of the population appears to have a clinically-silent form of thalassemia with increasing frequency.[10] In the Maghreb (African countries opening onto the Mediterranean), frequencies vary from 3% in Algeria to 7% in Morocco and Libya. In Egypt, thalassemia represents a serious health problem, with a predicted 1000 new patients born each year.[10] In Jordan, approximately 1000 cases of thalassemia major have currently been registered (1:4600 of the total population), with an annual increase of 80 cases, with 7–10% of the population believed to be carriers.[1] In northern Jordan, the overall prevalence of β-thalassemia is 5.93%, and the prevalence of β-thalassemia major is 0.1%.[4]

There is a wide distribution of thalassemia diseases in Syria. A total of 77 785 cases have been registered in different cities, but the disease is more common among Palestinian, Golan, and East Gouta residents.[11] In Damascus, according to 2008 screening, approximately 2593 cases of thalassemia major were diagnosed. However, the number of carriers is still unknown.[11]

Although β-thalassemia major is considered to be a common genetic disorder in Syria, there are few up-to-date research reports in the literature of the morphological and dimensional characteristics of the craniofacial compound, oral hygiene (risk of decay, gingivitis, and periodontal diseases), and the quality of life of affected patients. Therefore, the aim of this study was to investigate the oral manifestations and cephalometric craniofacial parameters (skeletal and dental) of β-thalassemic-major patients and to compare measurements with corresponding values in a group of unaffected patients.

Materials and methods

This study was approved by the council of Faculty of Dentistry, Damascus University, Damascus, Syria. A total of 51 (28 males and 23 females) thalassemic-major patients aged 8–12 years, from the Thalassemic Department of the Special Medical Care Center in Damascus, were asked to take part in this study. After obtaining informed consent from all children and their parents, orthodontic assessment was performed. All cooperative children who did not receive any previous orthodontic treatment were included in the study. Lateral cephalometric radiographs were taken using a standardized technique, with teeth in maximum occlusion and lips in a relaxed position, using Arcodent equipment (Fiad, Italy) with a magnification of ×1.3. Thirty-one linear and angular cephalometric parameters defining craniofacial morphology (23 skeletal and 8 dento-alveolar) were selected (Figures 1–3). The identification of landmarks was obtained by a principal investigator (MT). Angular and linear measurements were recorded to the nearest 0.5 and 0.5 mm, respectively. Ten

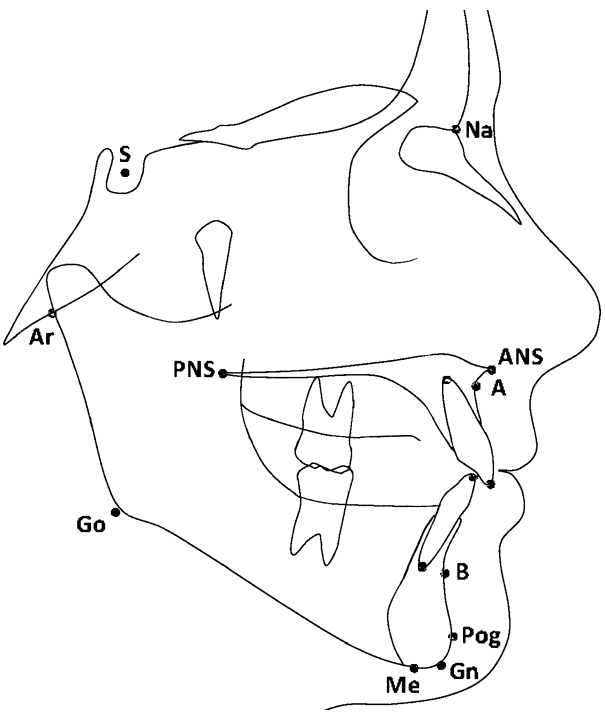

Figure 1. Points used in the cephalometric assessment. ANS, anterior nasal spine; Ar, articular; Gn, gnathion; Go, gonion; Me, menton; N, nasion; PNS, posterior nasal spine; Pog, pogonion; S, sella. A, A-point; B, B-point.

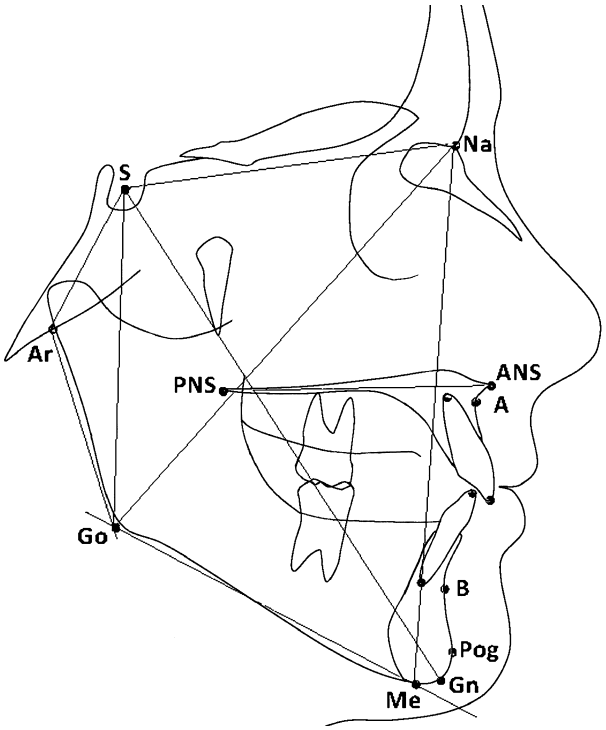

Figure 2. Linear measurements. Ar–Go, articular–gonian (ramus height); Go–Me, gonian–menton (mandibular body length); N–Go, nasion–gonian (facial depth); N–Me, nasion–menton (total anterior face height); S–Ar, sella–articulare (posterior cranial base length); S–Gn, sella–gnathion (facial length); S–Go, sella–gonian (total posterior face height); S–N, sella–nasion (anterior cranial base length).

randomly-selected cephalometric radiographs were remeasured to calculate the error in sella (S; midpoint of sella turcica)–articulare (Ar; point of intersection of the projection of the surface of the condylar neck and the inferior surface of the basi-occiput)–gonion (most posterior, inferior point on the angle of the mandible; Go), Ar–Go–menton (Me), A-point (deepest point on maxillary profile between the anterior nasal spine and the alveolar crest)–nasion (N; most anterior point on the frontonasal suture) B-point (deepest point on the concavity of the mandibular profile between the alveolar crest and the point of the chin) (ANB), anterior nasal spine (ANS)–posterior nasal spine (PNS): GoMe, LI: GoMe, S–gnathion (Gn), S–Go, N–Me, N–Go, and Go–Me measurements.

Angular and linear cephalometric parameters of 50 normal controls (26 males and 24 females) aged 8–12 years (9.44 ± 0.81) were obtained from a previous study undertaken at the Department of Orthodontics, Damascus University, to investigate Syrian norms. Controls were healthy Syrian children who did not previously receive orthodontic treatment and had normal occlusion, natural overbite, and overjet with no interdental spacing or crowding.[12]

The data obtained were analyzed using the Statistical Package for the Social Sciences (version 16; SPSS, Chicago, IL, USA). Descriptive statistics, including the mean, standard deviation, and differences between means for each group were computed. Reliability was tested by the intraclass correlation coefficient. The method was assessed using Dahlberg's formula: Error of method^2 = $\sum d^2/2n$, where d is the difference between two measurements and n is the number of double determinations.[13] The differences between thalassemic patients and controls were evaluated using the independent-group t-test. A P-value of ≤0.05 was considered to be statistically significant.

Results

Measurement error

The intraclass (intergroup) correlation coefficient, ranging from 86.9% to 99.9%, was statistically significant. The error of the method varied between 0.00 and 0.36 degrees for angular measurements and between 0.00 and 0.25 mm for linear measurements.

Sample characteristics

Fifty-one patients (28 males and 23 females) with β-thalassemia major and 50 controls (26 males and 24 females) aged 8–12 years were included in this study. The mean age of the thalassemic patients and healthy controls was 9.46 ± 1.21 and 9.44 ± 0.81, respectively. No significant difference was found between the mean age of thalassemic children and controls. The distribution of age and sex for healthy patients and children with β-thalassemia major is presented in Table 1. The mean and significance of the craniofacial features studied for thalassemic and control children are shown in Table 2.

Skeletal measurements

In general, the cranial base parameters appeared normal in thalassemic patients in the anterio-posterior plane. Also, no significant difference was noted between thalassemic and control children in relation to anterior and posterior cranial base lengths (S–N and S–Ar). Moreover, the thalassemic group had no significant ($P > 0.05$) maxillary prognathism, since the mean (S–N A-point; SNA) angle was normal (81.22 ± 2.51). However, thalassemic patients showed significant retrognathia in the mandible ($P < 0.0001$) with a reduced S–N B-point (SNB) angle (73.97 ± 2.98 degrees *vs* 77.48 ± 3.15 degrees in controls) and decreased S–N–pogonion (most anterior point on the bony chin; SNPog) angle (73.55 ± 2.86 degrees *vs* 77.90 ± 3.33 degrees in controls).

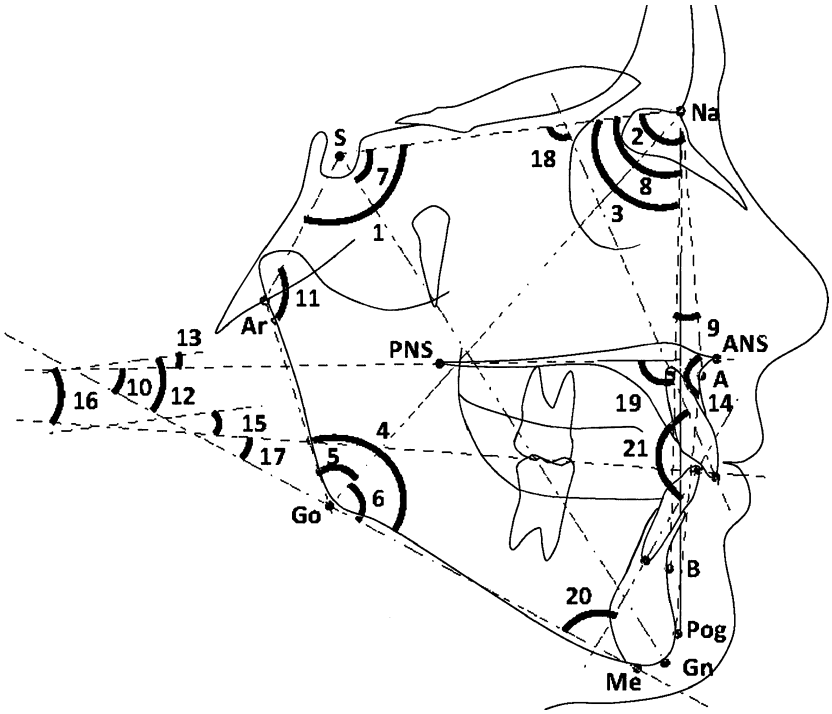

Figure 3. Angular measurements. Skeletal: 1, NSAr (nasion–sella–articulare); 2, SNA (sella–nasion A-point); 3, SNB (sella–nasion B-point); 4, ArGoMe (articulare–gonion–menton); 5, NGoAr (nasion–gonion–articulare); 6, NGoMe (nasion–gonion–menton); 7, NSGn (Y) (nasion–sella–gnathion); 8, SNPog (sella–nasion–pogonion); 9, ANB (A-point–nasion B-point); 10, ANS–PNS/GoMe (B) (anterior nasal spine–posterior nasal spine/gonion–menton) (basal plane angle); 11, SArGo (sella–articulare–gonion); 12, SN/GoMe (sella–nasion line–mandibular plane); 13, SN/ANS–PNS (sella–nasion line/anterior nasal spine–posterior nasal spine) (palatal plane); 14, NAPog (nasion A-point–pogonion). Dental: 15, SN/Ocp (sella–nasion line–occlusal plane); 16, ANS–PNS/Ocp (anterior nasal spine–posterior nasal spine/occlusal plane) (palatal plane); 17, GoMe/Ocp (gonian–menton/occlusal plane) (mandibular plane); 18, SN/UI (sell–nasion line–upper central incisor long axis); 19, ANS–PNS/UI (anterior nasal spine–posterior nasal spine/upper central incisor long axis) (palatal plane); 20, GoMe/LI (gonion-menton/lower central incisor long axis) (mandibular plane); 21, UI/LI (angle between the long axis of upper and lower central incisors).

Table 1. Sex distribution, means, and standard deviations (SD) of age for β-thalassemia major and healthy patients

Sample characteristics		Males	Females	Total
Thalassemic group	*n* (%)	28 (54.9%)	23 (45.1%)	51 (100%)
	Age (years): mean ± SD	9.57 ± 1.26	9.33 ± 1.16	9.46 ± 1.21
Control group	*n* (%)	26 (52.0%)	24 (48.0%)	50 (100%)
	Age (years) mean ± SD	9.57 ± 0.92	9.27 ± 0.63	9.44 ± 0.81

The thalassemic children also showed clockwise growth, as they had a significant increase in the mandible–ramus ArGoMe angle (128.23 ± 5.5 degrees *vs* 125.47 ± 4.50 degrees in controls, $P = 0.007$), increase in Go2 angle (75.92 ± 3.87 degrees *vs* 72.97 ± 2.57 degrees in controls, $P < 0.0001$), and increase in articular angle SArGo (147.75 ± 6.58 degrees *vs* 144.91 ± 4.92 degrees in controls, $P = 0.016$).

No significant difference was observed between the thalassemic group and controls with regards to mandibular body length (Go–Me) and facial depth (N–Go), while there was a highly-significant decrease in the ramus height (Ar–Go = 36.51 ± 3.87 mm *vs* 40.96 ± 2.88 mm, $P < 0.0001$), and a significant decrease in the facial length (S–Gn = 109.99 ± 5.41 mm *vs* 112.13 ± 4.04 mm, $P = 0.027$) in thalassemic patients when compared to controls.

A statistically-significant ($P < 0.0001$) class II skeletal pattern with a convex facial profile was also noted in children with thalassemia who had an increased nasion A-point–pogonion (NAPog) angle (194.90 ± 4.15 degrees *vs* 186.92 ± 4.57 degrees in controls) and an increased

Table 2. Means, standard deviations (SD), differences between means of all craniofacial parameters investigated, and significance for thalassemic and control children

Parameters	Thalassemia (n = 51) mean ± SD	Control (n = 50) mean ± SD	Independent groups t-test between means	Level of significance
Cranial base				
NSAr	124.64 ± 5.34	123.95 ± 4.47	0.70	0.48
S–N (m)	68.12 ± 3.26	67.72 ± 2.65	0.68	0.50
S–Ar (m)	31.01 ± 3.11	31.03 ± 2.31	0.04	0.97
Maxilla				
SNA	81.22 ± 2.51	81.12 ± 3.37	0.17	0.87
Mandible				
SNB	73.97 ± 2.98	77.48 ± 3.15	5.75	<0.0001
NGoAr (Go1)	52.26 ± 4.12	52.53 ± 3.27	0.36	0.72
NGoMe (Go2)	75.92 ± 3.87	72.97 ± 2.57	4.50	<0.0001
ArGoMe	128.23 ± 5.53	125.47 ± 4.50	2.75	0.007
SNPog	73.55 ± 2.86	77.90 ± 3.33	7.05	<0.0001
N–Go (m)	107.27 ± 6.78	107.44 ± 4.36	0.15	0.88
S–Gn (m)	109.99 ± 5.41	112.13 ± 4.04	2.25	0.027
Ar–Go (m)	36.51 ± 3.87	40.96 ± 2.88	6.55	<0.0001
Go–Me (m)	65.21 ± 4.40	65.75 ± 3.38	0.69	0.49
Maxillomandibular				
ANB	7.15 ± 2.02	3.64 ± 1.72	9.39	<0.0001
NAPog	194.90 ± 4.15	186.92 ± 4.57	9.19	<0.0001
Vertical skeletal				
SArGo	147.75 ± 6.58	144.91 ± 4.92	2.45	0.016
Björk	400.59 ± 4.87	394.34 ± 4.07	6.99	<0.0001
NSGn (Y)	71.83 ± 3.09	67.7 ± 3.30	6.49	<0.0001
NS/GoMe	40.78 ± 4.83	34.42 ± 4.01	7.19	<0.0001
NS/ANS–PNS	5.95 ± 2.91	8.62 ± 2.30	5.11	<0.0001
ANS–PNS/GoMe	34.91 ± 5.31	25.71 ± 4.02	9.80	<0.0001
S–Go (m)	64.24 ± 5.73	68.72 ± 3.39	4.65	<0.0001
N–Me (m)	110.78 ± 6.66	107.77 ± 4.49	2.66	0.009
Jarabak ratio	58.44 ± 4.00	63.82 ± 3.39	7.00	<0.0001
Dental				
NS/Ocp	22.94 ± 3.30	19.99 ± 3.14	4.60	<0.0001
ANS–PNS/Ocp	17.38 ± 4.00	11.42 ± 2.74	8.72	<0.0001
GoMe/Ocp	17.92 ± 4.12	14.50 ± 2.56	5.00	<0.0001
UI/SN	99.32 ± 6.59	103.16 ± 5.46	3.19	0.002
UI/ANS–PNS	105.07 ± 6.77	111.56 ± 4.62	5.62	<0.0001
LI/GoMe	100.51 ± 6.73	96.72 ± 4.72	3.27	0.0015
Interdental				
I/I	119.81 ± 8.32	126 ± 6.34	4.20	0.0001

ANB, A-point–nasion B-point; ANS, anterior nasal spine; Ar, articular; Gn, gnathion; Go, gonian; I/I, interincisor angle; LI, lower central incisor long axis; Me, menton; N, nasion; NAPog, nasion A-point–pogonion; Ocp, occlusal plane; PNS, posterior nasal spine; S, sella; SNA, sella–nasion A-point; SNB, sella–nasion B-point; SNPog, sella–nasion–pogonion; UI, upper central incisor long axis.

maxillomandibular ANB angle (7.15 ± 2.02 degrees *vs* 3.64 ± 1.72 degrees in controls).

In the vertical plane, thalassemic patients presented a posterior rotation of the mandible due to an increased facial axis (NSGn:*Y*-axis), Björk sum and craniomandibular planes (NS/GoMe) angles (71.83 ± 3.09 degrees, 400.59 ± 4.87 degrees, and 40.78 ± 4.83 degrees, respectively). The corresponding values in the controls were 67.7 ± 3.30 degrees, 394.34 ± 4.07 degrees, and 34.42 ± 4.01 degrees, respectively. These differences were highly significant ($P < 0.0001$).

Moreover, the thalassemic patients showed an anterior inclination of the maxillary plane with decreased NS/ANS–PNS angle (5.95 ± 2.91 degrees *vs* 8.62 ± 2.30 degrees in the control group). The difference of 5.11 degrees was highly significant ($P < 0.0001$). In addition, a skeletal open bite was also observed as the maxillary-mandibular plane (ANS–PNS/GoMe) angle was

Table 3. Means, standard deviations (SD), differences between means of all craniofacial parameters investigated, and significance for thalassemic males and females

Parameters	Females (n = 23) mean ± SD	Males (n = 28) mean ± SD	Independent groups t-test between means	Level of significance
Cranial base				
NSAr	125.35 ± 5.18	124.05 ± 5.49	0.86	0.39
S–N (m)	66.83 ± 2.06	69.18 ± 3.69	2.7	0.009
S–Ar (m)	29.78 ± 2.86	32.02 ± 2.98	2.7	0.009
Maxilla				
SNA	81.59 ± 2.23	80.91 ± 2.72	0.96	0.34
Mandible				
SNB	74.11 ± 2.90	73.86 ± 3.09	0.30	0.77
NGoAr (Go1)	52.13 ± 4.94	52.36 ± 3.39	0.20	0.85
GoMe (Go2)	75.78 ± 4.42	76.04 ± 3.44	0.24	0.81
ArGoMe	127.94 ± 6.25	128.46 ± 4.96	0.33	0.74
SNPog	73.72 ± 2.81	73.41 ± 2.95	0.38	0.70
N–Go (m)	105.50 ± 6.76	108.71 ± 6.57	1.71	0.093
S–Gn (m)	108.39 ± 4.05	111.30 ± 6.07	1.97	0.055
Ar–Go (m)	36.35 ± 4.22	36.64 ± 3.63	0.05	0.96
Go–Me (m)	65.52 ± 4.04	64.95 ± 4.72	0.46	0.65
Maxillomandibular				
ANB	7.44 ± 2.05	6.91 ± 2.00	0.93	0.36
NAPog	195.04 ± 3.97	194.79 ± 4.36	0.21	0.83
Vertical skeletal				
SArGo	147.61 ± 8.26	147.86 ± 4.96	0.13	0.89
Björk	400.91 ± 5.97	400.32 ± 3.88	0.43	0.67
NSGn (Y)	71.57 ± 3.14	72.05 ± 3.08	0.55	0.59
NS/GoMe	40.85 ± 5.91	40.73 ± 3.84	0.09	0.93
NS/ANS–PNS	6.15 ± 2.87	5.79 ± 2.98	0.44	0.66
ANS-PNS/GoMe	34.33 ± 5.99	35.39 ± 4.73	0.71	0.48
S–Go (m)	62.22 ± 6.67	65.89 ± 4.27	2.00	0.032
N–Me (m)	108.83 ± 5.28	112.39 ± 7.31	1.95	0.057
Jarabak ratio	58.01 ± 4.88	58.80 ± 3.07	0.45	0.63
Dental				
NS/Ocp	22.96 ± 3.77	22.93 ± 2.94	0.03	0.97
ANS-PNS/Ocp	17.30 ± 4.27	17.45 ± 3.84	0.13	0.90
GoMe/Ocp	17.89 ± 4.71	17.95 ± 3.64	0.05	0.96
UI/SN	100.35 ± 7.31	98.38 ± 5.85	1.07	0.29
UI/ANS–PNS	73.76 ± 7.16	76.00 ± 6.35	1.18	0.24
LI/GoMe	100.52 ± 7.38	100.50 ± 6.24	0.01	0.99
Interdental				
I/I	118.28 ± 8.98	121.22 ± 7.57	1.27	0.21

ANB, A-point–nasion B-point; ANS, anterior nasal spine; Ar, articular; Gn, gnathion; Go, gonian; I/I, interincisor angle; LI, lower central incisor long axis; Me, menton; N, nasion; NAPog, nasion A-point–pogonion; Ocp, occlusal plane; PNS, posterior nasal spine; S, sella; SNA, sella–nasion A-point; SNB, sella–nasion B-point; SNPog, sella–nasion–pogonion; UI, upper central incisor long axis.

significantly increased ($P < 0.0001$) in the thalassemic children (34.91 ± 5.31 degrees) when compared to the control group (25.71 ± 4.02 degrees).

Indeed, there was a decrease in the total posterior facial height (S–Go 64.24 ± 5.73 mm) and increase in the total anterior facial height (N–Me 110.78 ± 6.66 mm) in the thalassemic group when compared to the controls (68.72 ± 3.39 mm and 107.77 ± 4.49 mm, respectively) and the differences were highly significant ($P < 0.0001$ and $P = 0.009$, respectively). Also, the Jarabak ratio, which is the proportion of total posterior facial height (S–Go) to total anterior facial height (N–Me) was significantly ($P < 0.0001$) reduced in the thalassemic patients (58.44 ± 4.00%) when compared to the controls (63.82 ± 3.39%).

Dental measurements

A posterior rotation of the mandible in thalassemic patients was significantly noted ($P < 0.0001$), as the value

of the angle of occlusion-cranial planes NS/occlusal plane (Ocp; 22.94 ± 3.30), angle of the occlusion-maxillary plane ANS–PNS/Ocp (17.38 ± 4.00), and the angle of occlusion-mandible plane GoMe/Ocp (17.92 ± 4.12) were increased in the thalassemic patients in comparison to the controls.

The maxillary central incisors (upper central incisor long axis [UI]/SN, UI/ANS–PNS) were retroclined in the thalassemic patients (99.32 ± 6.59 degrees and 105.07 ± 6.77 degrees, respectively) when compared to the control group (103.16 ± 5.46 degrees and 111.56 ± 4.62 degrees, respectively) with highly-significant differences ($P = 0.002$ and $P < 0.0001$, respectively). In contrast, mandibular central incisors (lower central incisor long axis [LI]/GoMe) were significantly proclined in the thalassemic patients when compared to the controls (100.51 ± 6.73 degrees *vs* 96.72 ± 4.72 degrees in the controls, $P = 0.0015$). A labial proclination for anterior incisors was also observed as the interincisor angle (I/I) (lower central incisor long axis, upper central incisor long axis) was more reduced in the thalassemic group than in the controls (119.81 ± 8.32 degrees *vs* 126 ± 6.34 degrees in the controls), and the difference was highly significant ($P = 0.0001$).

The mean and significance of the craniofacial features of the thalassemic males ($n = 28$) and females ($n = 24$) were also investigated. Findings are presented in Table 3. There was no significant difference between the thalassemic males and females in relation to all angular measurements studied. However, a significantly shorter ($P = 0.009$) anterior cranial base lengths (S–N) was observed in the thalassemic females than in the thalassemic males (66.83 ± 2.06 mm *vs* 69.18 ± 3.69 mm). Similarly, a significantly shorter ($P = 0.009$) posterior cranial base lengths (S–Ar) was noted in the thalassemic females than in the thalassemic males (29.78 ± 2.86 mm *vs* 32.02 ± 2.98 mm).

In addition, the thalassemic females showed a significant decrease ($P = 0.032$) in the total posterior facial height S–Go (62.22 ± 6.67 mm) when compared to males (65.89 ± 4.27 mm). However, a marginally-significant decrease ($P = 0.057$) in the total anterior facial height (N–Me) was noted in the thalassemic females (108.83 ± 5.28 mm) when compared to the males (112.39 ± 7.31 mm).

Discussion

Thalassemia is a hereditary, common disease in Syria. The disease poses a great challenge to the health-related quality of life of children.[14] It was suggested that improved knowledge of craniofacial and other oral manifestations of thalassemic patients would be essential for developing more suitable clinical, psychological, and social support programs that might improve the treatment outcomes of these patients. In light of the limited research in this area, this study was undertaken to investigate characteristics and craniofacial parameters of thalassemic children aged 8–12 years.

Previous studies have investigated craniofacial manifestations and the possibility for orthodontic treatment in thalassemic patients.[7,15,16] Some investigators have reported a successful surgical correction of the maxilla.[7] Others encouraged early orthodontic treatment in thalassemic patients, and concluded that the disease factor of thalassemia does not interfere with osteoclastic and osteoblstic activity that occurs with orthodontic tooth movement.[15]

The present study found normal cranial angular and linear measurements (NSAr, S–N, S–Ar) in Syrian thalassemic patients aged 8–12 years. Previously, Amini *et al.*[8] found no significant difference between Iranian thalassemic patients (mean: 10.4 ± 4.29 years) and controls in relation to cranial base measurements. However, Bassimitci *et al.*,[17] who investigated 30 Turkish thalassemic individuals and 30 controls (mean: 10.84 ± 3.49 years), demonstrated a reduced saddle angle (NSAr) with a short posterior cranial base length from the sella turcica to the Ar point. Similarly, Abu Alhaija *et al.*[15] reported a highly-significant reduction in angular and linear dimensions of the cranial base in 54 Jordanian thalassemic children aged 5.5–16 years.

Our study has shown a normal position of the maxilla in the sagittal plane (SNA = 81.22) in the thalassemic group. This is in agreement with other studies, which have reported insignificant sagittal overgrowth of the maxilla in thalassemic patients.[8,17] However, these findings are inconsistent with those reported, in that thalassemic patients exhibit an obvious protrusion of the maxilla due to hypertrophy of maxillary erythroid marrow.[5,15,18–20]

It should be emphasized that studies that have investigated thalassemic patients, rather than thalassemic and controls from the same population, might explain the disagreement with our results.

The cephalometric analysis in the present study showed that the mandible in the thalassemic patients tended to be retrognathic, with a posterior position of the chin (reduced SNB and SNPog). Similar findings were also reported by Bassimitci *et al.*[17] and Amini *et al.*,[8] who found that the mandible appeared to be more retruded in thalassemic patients. Abu Alhaija *et al.*[15] reported a normal rather than retruded position of the mandible in thalassemic patients in the horizontal plane.

Our results are in agreement with two studies undertaken by Bassimitci *et al.*[17] and Amini *et al.*,[8] who reported a strong vertical (clockwise) growth associated with skeletal open bite (increased SArGo, ArGoMe, Go2, and ANS–PNS/GoMe) in thalassemic children,[8,17] but were different from the findings of these two studies in that we noted

normal facial depth (N–Go) and normal mandibular body length (Go–Me) in our thalassemic patients.[8,17]

Our findings were in agreement with previous work[8,15] that demonstrated a decrease in the total and lower posterior facial heights (S–Go, Ar–Go) in thalassemic patients due to the reduced ramus and deficient growth of the condyles. However, our finding were different from those reported by Bassimitci *et al.*,[17] who found no significant differences between the thalassemic group and controls in the measurements of total and lower posterior facial heights.

The present study showed that the thalassemic patients had a class II skeletal pattern complicated by a more convex long facial profile (increased NAPog and ANB). This is in accordance with the findings of Amini *et al.*,[8] Bassimitci *et al.*,[17] and Abu Alhaija *et al.*,[15] who reported a marked convexity of the lower face associated with large, intermaxillary discrepancy in thalassemic patients.

Bassimitci *et al.*[17] found a posterior rotation of the mandible in thalassemic individuals. Similarly, we found a posterior (clockwise) mandibular rotation in the thalassemic children (increased NSGn:*Y*-axis, Björk, NS/GoMe).

Our study demonstrated an enlargement of the maxilla in the vertical plane (decreased NS/ANS–PNS) and anterior (anticlockwise) inclination of the maxilla. Bassimitci *et al.*[17] previously found an anterior inclination of the maxilla, and they attributed this to the enlargement of the maxillary marrow spaces. In contrast, our findings are different from those reported by Amini *et al.*,[8] who did not find a significant anticlockwise inclination (1.4) of the palatal plane. It is worth mentioning that the posterior rotation of the mandible, together with the anterior (anticlockwise) inclination of the maxilla, might be a direct reason for the presented skeletal anterior open bite in thalassemic-major patients.

The increased total anterior facial height (N–Me) and the reduced Jarabak ratio (S–Go/N–Me) noted for our thalassemic patients suggest a severe vertical growth pattern and long facial profile. These findings are consistent with those reported by Bassimitci *et al.*[17] and Amini *et al.*,[8] who found an increase of lower anterior facial height, indicating a vertical growth pattern of the mandible. Abu Alhaija *et al.*[15] found an increase in the lower anterior facial height in the stage 3 thalassemic group (mean age: 13.8 ± 1.44 years) and a reduced total anterior facial height (N–Me) in the stage 1 group with thalassemia (mean age: 7.5 ± 1.09 years).

In agreement with results of previous works,[8,17] thalassemic children showed retroclined upper incisors (UI/SN and UI/ANS–PNS) and proclined lower incisors (LI/GoMe), indicative of incisors compensation. Our results were also in agreement with those of Abu Alhaija *et al.*,[15] who showed normal inclination of lower incisors and found that upper incisors tended to be upright or even retroclined in some cases.

Similarly, a reduced I/I angle associated with severe protrusion of anterior teeth was observed in thalassemic-major patients. Retroclined maxillary incisors were considered proclined due to the anterior inclination of the maxilla and the increase of maxillary/occlusal and maxillary/mandibular angles. Similar to our results, Bassimitci *et al.*[17] and Amini *et al.*[8] attributed these findings to the overeruption of the lower and upper incisors as a result of the marked increase in the lower facial height (vertical growth pattern) in thalassemic patients.

No significant difference was found between the thalassemic males and females in relation to all angular measurements investigated. Our study confirmed shorter anterior and posterior cranial base lengths (S–N) in the thalassemic females than in the thalassemic males (S–Ar). Bassimitci *et al.*,[17] who had similar findings, attributed linear differences to the variation of skeletal development between males and females in the same age group.

In conclusion, this study has shown that Syrian thalassemic children developed a skeletal class II malocclusion subsequent to posterior rotation and retrognathia of the mandible, accompanied by short height of the ramus and anterior inclination of the maxilla. The study has also confirmed vertical facial growth, and increased anterior and reduced posterior facial heights in thalassemic children. This study has improved understanding about craniofacial characteristics of Syrian children with thalassemia. Further studies with a larger sample size are needed to ascertain these finding. Longitudinal studies are also essential to determine the craniofacial parameters and the amount of growth of thalassemic patients from childhood into adulthood. Patients with thalassemia who have severe malocclusion and esthetic impairments might have worse oral health-related quality of life than normal children. Therefore, our study is still in progress to investigate the oral health-related quality of life of thalassemic patients. This might hold promise in delivering the best oral health care to this medically-compromised group.

Acknowledgments

The authors are grateful to the thalassemic patients and their parents for their help in the study. The authors would also like to thank Dr Kusai Al-Zir, Dr Rania Hadad, Dr Mhd.Wasseem Al-Lahham, Dr Humam Saltaji, and Dr Mayssa Al-Salti (all from the Faculty of Dentistry, Damascus University) for their invaluable assistance. This study was funded by Damascus University, Damascus, Syria.

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